Remarks

Claims 14-29, 35, 36, and 39-47 are pending.

Rejection Under 35 U.S.C. § 102

Claims 14-18, 20-29, 35, 36, and 39 are rejected under 35 U.S.C. § 102(e) as anticipated by U.S. Patent No. 6,692,456 to Eppstein, et al. ("Eppstein"). The rejection is respectfully traversed for the reasons articulated below.

The Rejection is Not Based on Proper Legal Standards

The Office Action fails to show that Eppstein discloses each and every element of Applicants' claims 14-18, 20-29, 35, 36, and 39, because Eppstein does not disclose the required "*means for rupturing* the rupturable covering *and positively displacing* the release formulation through the opening at the first end."

A proper *prima facie* case of equivalence has not been made. An element in a claim expressed as a means for performing a specified function "shall be construed to cover the corresponding structure, material, or acts described in the specification or equivalents thereof." 35 U.S.C. § 112, ¶ 6. "Accordingly, the PTO may not disregard the structure disclosed in the specification corresponding to such language when rendering a patentability determination." In re Donaldson Co., 16 F.3d 1189, 1195 (Fed. Cir. 1994). In making a *prima facie* case of equivalence, "the Examiner should provide an explanation and rationale in the Office Action as to why the prior art element is an equivalent." M.P.E.P. § 2183. Importantly, the application of a prior art reference to a means plus function claim *requires* that the prior art element perform the *identical function* specified in the claim. M.P.E.P. § 2182.

Applicants' Claimed Device Functions in Distinct Manner from Eppstein's Device

Applicants' claimed devices specifically require a means for *positively displacing* the release formulation. Advantageously, the positive displacement may increase the release rate relative to release by passive diffusion (see Pg. 6, Lns. 21-25). In fact, such release kinetics may be necessary, for example, in releasing drugs whose efficacy is dependent on a fast pharmacokinetic pulsatile profile (Pg. 6, Lns. 25-28). Applicants' specification describes these means as including, in exemplary embodiments, a fluid or heat swellable material. As specified in the claims, the function of these means is to *positively displace* the release formulation out of the reservoir/device.

In contrast, Eppstein teaches devices for forming openings in biological membranes and delivering fluid therethrough using "pressure modulation links" "(a)" (Col. 31, Lns. 19-23; Fig. 24). Specifically, the central pressure modulation links are pressed down relative to the outer links to compress the skin, and then the central links are pulled back while the outer links are pressed down to *induce* fluid to flow from the reservoir and into the skin (Col. 31, Lns. 19-28; Fig. 22). Such inducement is not positive displacement.

The fluid in Eppstein's device is not positively displaced from the reservoir, as positive displacement requires that the space occupied by the fluid in the reservoir be eliminated (e.g., by reducing the dimensions and thus volume of the reservoir) or that the fluid be pushed out by another material (e.g., an expandable material) such that the fluid physically cannot remain in or return to the reservoir. In Eppstein, the reservoir volume is fixed and is not displaced by another material. Accordingly, Eppstein does not teach or suggest a means for positively displacing a

release formulation. In addition, Eppstein does not teach or suggest a means that includes a fluid or heat swellable material.

Nothing in Eppstein Is Equivalent to Applicants' Claimed

Means for Rupturing and for Positively Displacing.

Nothing in Eppstein can reasonably be construed as equivalent to Applicants' means *for rupturing* the rupturable covering *and positively displacing* the release formulation. First, "unless an element performs the identical function specified in the claim, it *cannot* be an equivalent." M.P.E.P. § 2184 [II]. While the pyrotechnic element of Eppstein may provide a rupture function, it has no positive displacement function on the release formulation. Because neither the pressure modulation links nor any other structure in Eppstein performs the function of positively displacing a release formulation, they *cannot* be equivalent to Applicants' means for functionally displacing the release formulation.

The Office Action, at page 2, alleges that Fig. 24 of Eppstein teaches a means "(e)" for rupturing a covering and positively displacing a release formulation. This is incorrect. Means "(e)" comprises a thermal poration element (Fig. 23a; Col. 31, Lns. 13-16). Eppstein teaches that thermal poration elements may porate the surface of the skin and simultaneously breach the lower surface of the reservoir (Col. 25, Lns. 36-39). Thermal poration element "(e)" clearly does not perform the function of positively displacing a release formulation. Accordingly, a proper *prima facie* case of equivalence has not been made.

Moreover, nothing in Eppstein can reasonably be construed as supporting a *prima facie* conclusion of equivalence. Factors sufficient to support a *prima facie* conclusion of equivalence include: (a) whether the prior art element performs the identical function specified in the claim in

substantially the same way; (b) whether a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding element disclosed in the specification; (c) whether there are insubstantial differences between the prior art element and the corresponding element disclosed in the specification; and (d) whether the prior art element is a structural equivalent of the corresponding element disclosed in the specification. M.P.E.P. § 2184 [II]. With respect to factor (a), Eppstein's pressure modulation system does *not* perform the "positively displacing" function specified in Applicants' claims, and plainly does function in the same way. As to factor (b), a person of ordinary skill would have recognized that Eppstein's pressure modulation system is *not* interchangeable with Applicants' claimed means, since the pressure modulation system only can be used in close proximity to a biological membrane. As to factors (c) and (d), there are substantial differences, both structural and functional, between a pressure modulation system and Applicants' claimed means which, in some embodiments, includes a fluid or heat swellable material. For example, the structure and function of Eppstein's device provides and relies upon microporation of a biological membrane. In contrast, Applicants' claimed device does not require such functionality or structure.

For these reasons, no *prima facie* case of anticipation has been established in view of Eppstein. Applicants' claims 14-18, 20-29, 35, 36, and 39 are therefore novel over Eppstein.

Rejection Under 35 U.S.C. § 103

Claims 19 and 42-47 are rejected under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 7,025,323 to Krulevitch, et al. ("Krulevitch") in view of U.S. Patent No. 5,797,898 to Santini Jr., et al. ("Santini"). Claims 40 and 41 are rejected as obvious over Eppstein in view of U.S. Patent No. 4,111,202 to Theeuwes ("Theeuwes"). These rejections are respectfully traversed.

The Combination of Krulevitch and Santini Fails to Teach

Or Suggest All Claimed Features of Applicants' Claim 19.

Neither Krulevitch nor Santini teaches or suggests a device in which a release formulation is disposed and wholly contained within *a reservoir that is defined inside a microtube*. In both Krulevitch and Santini, the reservoir is located in a substrate that is not a microtube. Neither reference suggests having a release formulation disposed wholly within the microtube reservoir, as required by Applicants' claim 19.

The Office Action, at page 3, alleges that "Krulevitch teaches an array of discrete microtubes (97) *defining* a reservoir (86-90)..." (emphasis added). This is simply incorrect. As Applicants pointed out in their remarks filed May 11, 2007, microneedles 97 do not in any reasonable way "define" reservoirs 86-90. Moreover, the formulation reservoirs in Krulevitch are *remote from* the microneedles. It does not teach locating reservoirs within the microneedles. That is, Krulevitch does not teach a microtube having a formulation storage reservoir defined therein, as required by Applicants' claims.

The Final Office Action fails to refute and provides no reasonable explanation how Krulevitch is alleged to meet this feature required by claim 19. The examination record indicates that the Examiner failed to consider a feature of claim 19 which properly is entitled to patentable weight. The rejection is therefore improper and should be withdrawn.

The Rejection Is Improperly Premised Upon Insufficient Grounds

For Combining Krulevitch and Santini.

Krulevitch fails to disclose or suggest that one could or should provide a rupturable covering enclosing a first end of a reservoir in the microtube. Santini does not teach anything

about microneedles or microtubes. Moroever, it does not teach or suggest anything about *whether or how one of ordinary skill in the pertinent art would* place a rupturable covering over the end of a microtube.

"A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon ex post reasoning." KSR Int' l Co. v. Teleflex Inc., 550 U.S. ___ (2007) (Slip Op. at 17). The Examiner contends that it would have been obvious in view of Santini to place a metallic covering over the microneedles of Krulevitch in order to "prevent leakage of the reservoirs or contamination of the reservoirs contents" (Office Action, p. 3) or so that "the device of Krulevitch would no longer be limited to molecules of a certain charge" (Office Action, p. 5). This is hindsight-driven conjecture, unsupported by any objective evidence.

The U.S. Supreme Court recently stated that "a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." KSR Int'l Co. v. Teleflex Inc., 550 U.S. ___ (2007) (Slip Op. at 14). The Court further stated that "it will be necessary … to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an **apparent** reason to combine the known elements **in the fashion claimed**..." Id. The rejection here is based upon reasons that neither are *apparent* nor suggest combining the elements of Santini and Krulevitch in the *precise fashion claimed.*

The Court further intimates that a combination of elements may be obvious to try only "when there is a *design need or market pressure* to solve a problem and there are a **finite**

number of *identified, predictable solutions* [and] a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp" Id. at 6. In the instant case, a person of ordinary skill in the art trying to prevent contamination or carry molecules of a certain charge—the hypothetical problems or reasons imagined by the Examiner—has a *nearly infinite variety of technical options to choose from in try to meet such objectives*. For instance, the contamination means may be a seal located at the reservoir or at either or both ends of the microneedles, the means may utilize a mechanical or electromechanical valve, the means may focus on the formulation itself (e.g., making it less fluid), or the means may involve rupturable or non-rupturable materials and operational designs, just to name of few of the myriad variables one skilled in the art might or might not utilize depending on a host of engineering and practical considerations. Accordingly, it would have required more than mere common sense for the artisan of ordinary skill to leap from the prior art teachings of Krulevitch, alone or in combination with Santini, to derive Applicants' particular claimed devices.

In fact, it is apparent that the combination posited by the Examiner is only obtained using ex post reasoning, because Krulevitch teaches completely different methods of both sealing, which would prevent contamination, and using molecules of a particular charge. Specifically, Krulevitch teaches that "channel sealing is *dependent* on selective poly (dimethylsiloxane) (PDMS) surface modifications," and that "[t]he polymer channel should be hydrophobic and pneumatic fluid should be hydrophilic when using hydrophilic reagents *or vice versa*... for [a] leak proof seal." (Col. 6, Lns. 56-60) (emphasis added). Because Krulevitch teaches sealing molecules that are either hydrophilic or hydrophobic by the use of a specific type of *polymer*

located *in the substrate/channel structures,* it **teaches away** from sealing with a *metallic* cover at the *end of the microneedle.*

Claims 40 and 41 Are Not Obvious Over Eppstein in View of Theeuwes.

Nothing in Theeuwes remotely suggests a device having an array of discrete microtubes, a device constructed with a metal or an alloy, or a device with a rupturable covering. One of ordinary skill in the art would have had no reason to combine Theeuwes with Eppstein. The Examiner contends that it would have been obvious to combine the "osmotic delivery system of Theeuwes with the microneedle array of Eppstein in order to facilitate expansion of the expandable member without electronics." This ex post reasoning not only is unsupported conjecture, it also is irrelevant to the claims and primary references.

Eppstein does not teach operating a device by permitting selected molecules from outside the reservoir to diffuse to an expanding material to cause the expanding material to expand and displace the release formulation in an amount effective to rupture the rupturable covering and discharge the release formulation from the reservoir. In fact, Eppstein does not teach *any* use of *any* expanding material. The Examiner has identified no evidence to suggest a specific market or design need to modify the teachings of Eppstein to omit electronics from the device. Moreover, Applicants' claimed devices do not necessarily operate without electronics. Indeed, the Examiner has failed to articulate with any specificity why or how one of ordinary skill in the art would have been led to modify Eppstein's delivery device (which uses "pressure modulation activation links" to repeatedly *modulate* pressure in a plurality of microreservoirs) to somehow substitute an osmotic delivery system, which provides *continuous* pressure. It is not predictable that one could achieve with the Theeuwes osmotic system the same control of release kinetics

obtainable with the actuation means of Eppstein's device. Therefore, a person of ordinary skill in the art simply would not have combined Theeuwes with Eppstein for the reason alleged by the Examiner.

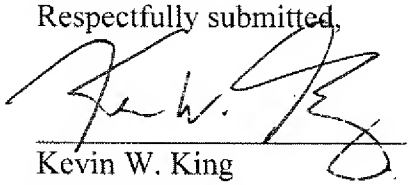
Moreover, Theeuwes fails to supplement the other deficiencies of Eppstein to meet all elements defining Applicants' claimed devices and methods. Accordingly, the combination of Theeuwes and Eppstein fails to establish a *prima facie* case of obviousness.

Conclusions

For the foregoing reasons, it is submitted that all of Applicants' claims are novel and non-obvious over the cited prior art. Prompt allowance of each of pending claims 14-29, 35, 36, and 39-47 is therefore respectfully solicited.

The undersigned kindly invites the Examiner to contact him by telephone (404.853.8068) if any outstanding issues can be resolved by conference or examiner's amendment.

Respectfully submitted,



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